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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/765,790	01/27/2004	Chris Beard	2035(301412)	2976

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SIEMENS CORPORATION
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EXAMINER	
BAUSCH, SARAE L	
ART UNIT	**PAPER NUMBER**
1634	

MAIL DATE	DELIVERY MODE
12/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/765,790	BEARD ET AL.	
	Examiner	Art Unit	
	Sarae Bausch, PhD	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 28-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 28-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 1, 3, 28-30 are pending in the instant application. Claims 2 and 4-27 have been canceled. Claim 1 has been amended while claims 28-30 have been added. This action is written in response to applicant's correspondence submitted 10/10/2008. All the amendments and arguments have been thoroughly reviewed but were found insufficient to place the instantly examined claims in condition for allowance. The following rejections are either newly presented, as necessitated by amendment, or are reiterated from the previous office action. Any rejections not reiterated in this action have been withdrawn as necessitated by applicant's amendments to the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is Final.**

Election/Restrictions

2. Applicant's election of group I (claims 1-4) in the reply filed on 01/17/2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

New Grounds of Rejection

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 3, 28-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Cameron et al. (Nature Genetics, 1999, vol. 21, p. 103-107). This is a new grounds of rejection, necessitated by the amendment to the claims.

With regard to claim 1 and 29, Cameron et al. teach that MLH1 and TIMP3 expression is silenced compared to normal cells. Cameron et al. teach comparing expression levels of MLH1 and TIMP3 with MLH1 and TIMP3 that have been demethylated and teach that the expression increases four fold (claim 29) (see pg. 104, 1st column, 1st full para cont'd to 2nd column 1st para and figure 2). Therefore, Cameron et al. teach identifying nucleic acid sequence that increase in expression after demethylation treatment and are useful as biomarker for cancer.

With regard to claim 3, Cameron et al. teach the promoter-exon region of TIMP3 is from -200 bp to +300 bp (see figure 3b) thus the promoter-exon region spans 1000 bases upstream and 1000 bases downstream.

With regard to claim 28 and 30, Cameron et al. teach analysis of TIMP3 expression in colorectal carcinoma cell line RKO, thus the diseased cell is from colon and disease is colorectal cancer (see pg. 103, 1st column, 1st para).

5. Claims 1, 3, 28-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Suh et al. (J. Biol. Chem, 2002, vol. 227, pp. 35795-35800). This is a new grounds of rejection, necessitated by the amendment to the claims.

With regard to claim 1 and 29, Suh et al. teach analysis of the promoter-first exon region in CDX1 gene (See figure 3). Suh et al. teach analysis and comparison of expression levels of CDX1 gene in both colorectal cell lines and control cell lines (see figure 2 and pg. 35797,

hypermethylation of CDX1 promoter correlates with absence of CDX1 expression in colorectal cancer cell lines). Suh et al. teach inducing expression by 11 and 20 fold due to demethylation after treatment with 5-azaC of the region -600 to +75 of the promoter-exon region of CDX1 (identifying nucleic acid sequences exhibiting a significant increase in expression after demethylation treatment) (see pg. 35798, Demethylation Activates the CDX1 Gene Promoter in SW480 Stable Clones and figure 3).

With regard to claim 3, Suh et al. teach analysis of the promoter-exon region that spans -600 to + 75 (see pg. 35798, 2nd column, 1st para).

With regard to claim 28 and 30, Suh et al. teach analysis of colorectal cancer cell lines (see pg. 35795, 2nd column, 2nd last para).

Maintained Rejection

6. Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Daskalakis et al. (Blood, Oct 2002, Vol. 100, pp. 2957-2964) as evidence by Leukemia and Lymphoma Society, Myelodysplastic Syndrome, pp. 1-4. This rejection was previously presented in section 12 of the office action mailed 06/20/2008 and has been rewritten to address the amendment to the claims.

With regard to claim 1, Daskalakis et al. teach low expression of p15 in biopsies from 10 myelodypastic syndrome (MDS) patients compared to 5 healthy individuals (see pg.2961, 2nd column, last paragraph). Daskalakis et al. teach the under-expression of p15 is associated with hypermethylation in the 5' region between positions –47 to +215 (see table 1 and pg. 2958, 2nd

column, 1st paragraph) (identifying one or more nucleic acid sequences that are down regulated in disease cells compared to normal cells wherein the nucleic acid sequences comprise at least one methylated CpG site in a promoter-first exon region). Daskalakis et al. teach comparison of expression level of p15 before and after treatment with decitabine (demethylation agent) (see figure 6) (comparing expression level of nucleic acid sequence with expression level of nucleic acid sequence that have been demethylated). Daskalakis et al. teach up regulation of p15 after demethylation during decitabine treatment (see figure 6) (identifying nucleic acid sequence exhibiting significant increase in expression level after demethylation treatment as compared to expression level of the same nucleic acid sequence in the methylated state).

With regard to claim 3, Daskalakis et al. teach hypermethylation spans the 5' region of p15, which encompass –47 to +215 (region that is within the range of 1000 base pairs upstream of the first exon and about 1000 base pair downstream of first exon) (see pg. 2958, 2nd column, 1st two paragraph and figure 5). Therefore, Daskalakis et al. teach identification of one CpG site within a promoter-first exon region that is within 1000 base pairs upstream of the first exon and about 1000 base pairs downstream of the first exon.

It is noted that Daskalakis teach comparison of methylation patterns in patients with myelodyplastic syndrome. Although, Daskalakis does not teach that myelodyplastic syndrome is cancer, the leukemia and lymphoma society define the disease as a blood cancer (see pg. 1). Therefore, Daskalakis teach analysis of biomarker for a disease that is cancer.

Response to Arguments

7. The response traverses the rejection on page 6 of the remarks mailed 10/10/2008. The response asserts that Daskalakis does not teach or suggest methods of biomarkers where the

disease is cancer. This response has been thoroughly reviewed but not found persuasive. It is noted, as described above, that Daskalakis teach a biomarker, p15, in MDS patients and MDS is a blood cancer, as defined by the Leukemia and Lymphoma society. Therefore, Daskalakis anticipates the claimed invention.

Conclusion

8. No claims are allowable.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarae Bausch, PhD whose telephone number is (571)272-2912. The examiner can normally be reached on M-F 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Sarae Bausch/
Primary Examiner
Art Unit 1634